DRUG REACTIONS

Dr.ZAIB AHMAD
MCPS(MED.)
FCPS (DERM.)

Cutaneous Drug Reactions

Table 7. Drugs Commonly Implicated In Cutaneous Allergic Reactions.

- Aminopenicillins
- Sulfonamides
- Cephalosporins
- Allopurinol
- Phenobarbital
- NSAIDs
- Quinolones
- Phenytoin
- Valproic acid
- ACE inhibitors
- Thiazide diuretics
- Beta-blockers
- Oral contraceptives
- Phenothiazines
- Corticosteroids

Cutaneous Drug Reactions

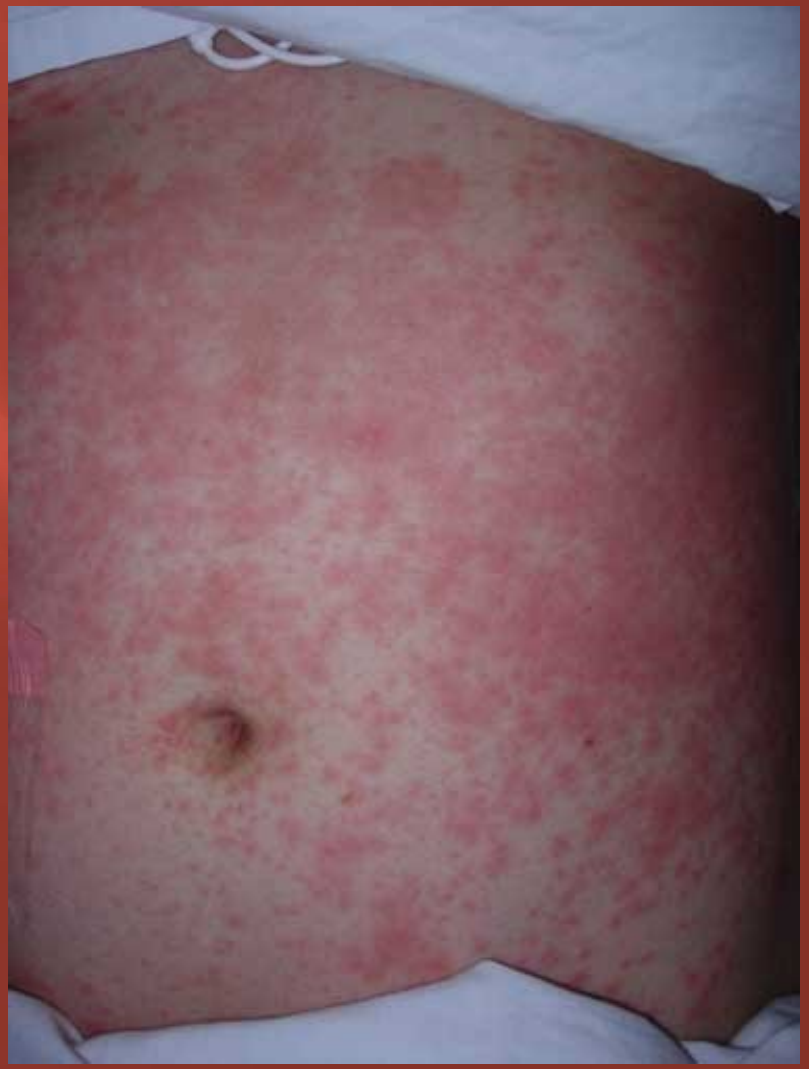
- Clinical Presentation
  - Most cutaneous drug eruptions are morbilliform (meaning it looks like measles) or exanthematous

Drug-induced Exanthems

- Morbilliform, maculopapular eruptions.
- Often associated with pruritis, low-grade fever, eosinophilia.
- Onset within 2 weeks of starting a new drug, or within days of re-exposure.
- Treatment is dicontinuation of the drug. Antihistamines, topical steroids, and topical antipruritics may also help.
- Usually begin in dependent areas and generalize.

Cutaneous Drug Reactions

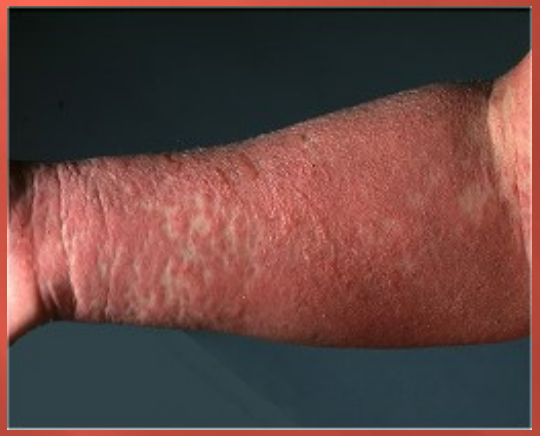
- Diagnosis
  - clinical



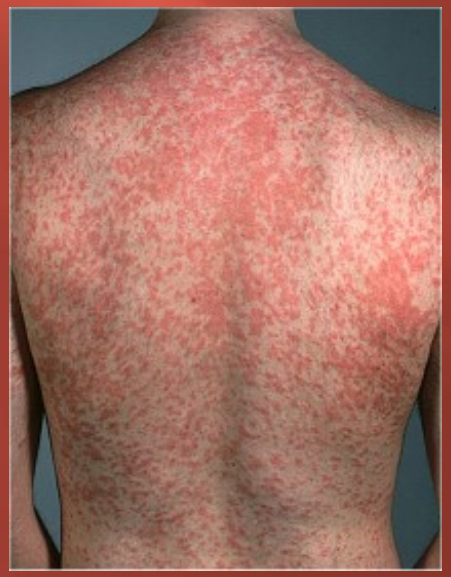
Exanthems

- T-cells recognize the drug and exert, depending on their function, a specific pathology

Bullous Exanthem



Maculopapular exanthem (MPE)



Acute generalized exanthematous pustulosis (AGEP)

Cutaneous Drug Reactions

- Treatment
  - Removing the drug
  - If possible, all drug therapy should be stopped
  - Routine use of corticosteroids is not indicated
  - Oral antihistamines (diphenhydramine 25-50 mg PO q6h prn) may alleviate pruritus

Erythema Multiforme, Stevens-Johnson Syndrome, And Toxic Epidermal Necrolysis

Table 8. Classification Of Erythema Multiforme, Stevens-Johnson Syndrome, And Toxic Epidermal Necrolysis.

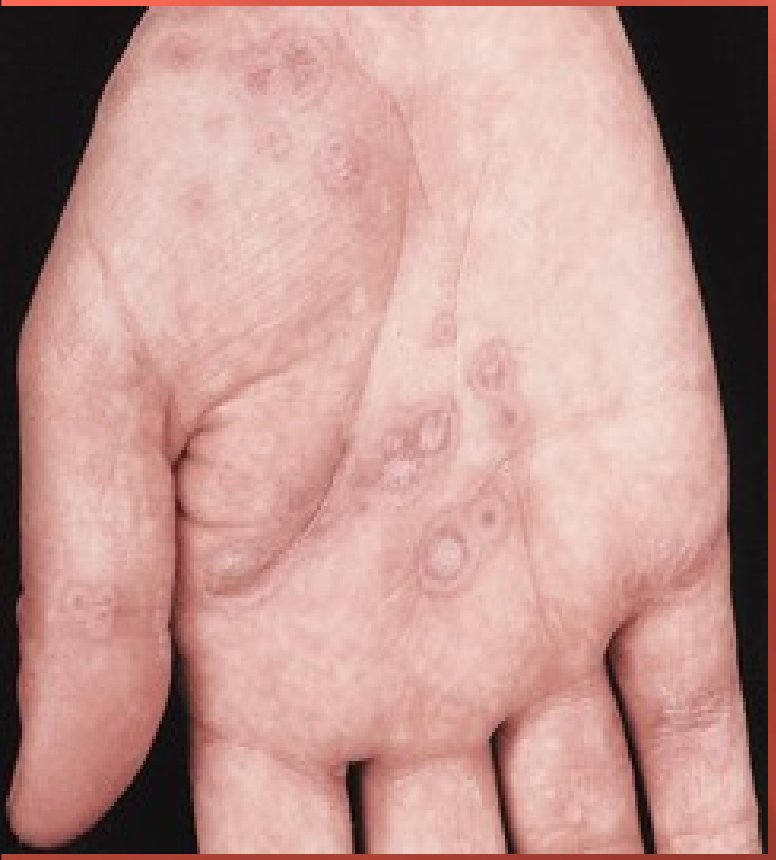
Entity	Most common etiologic agent/rash
Erythema multiforme minor	Infectious/classic target lesion without mucous membrane involvement (no epidermal detachment)
Erythema multiforme major	Infectious/classic target lesions with mucous membrane involvement (no epidermal detachment)
Stevens-Johnson syndrome	Drug induced/widespread purpuric macules and mucosal erosions with 10% epidermal detachment, plus Nikolsky's sign
SJS/TEN transition	Drug induced/widespread purpuric macules and mucosal erosions with 10%-30% epidermal detachment, plus Nikolsky's sign
Toxic epidermal necrolysis	Drug induced/widespread purpuric macules and mucosal erosions with more than 30% epidermal detachment, plus Nikolsky's sign

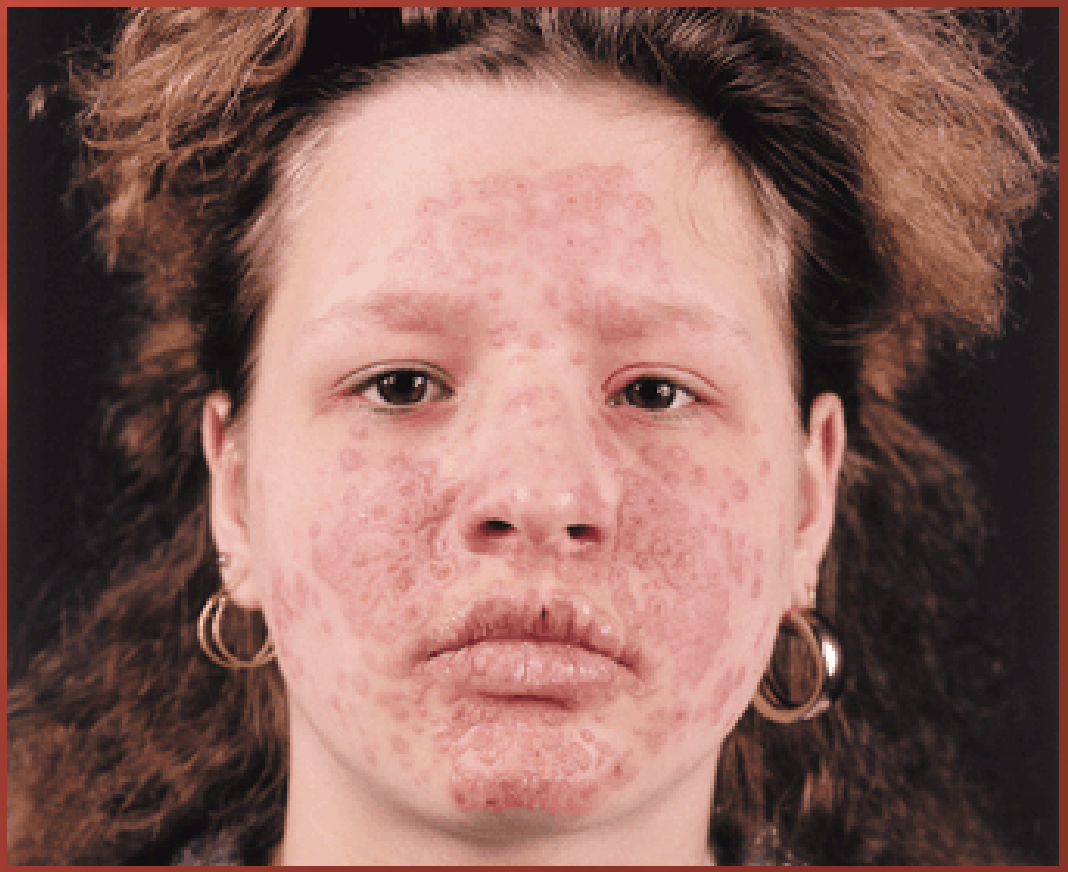
Erythema Multiforme

- Etiology
  - EM is a common acute inflammatory disease that is usually self-limited
  - in up to 50% of cases no etiologic agent can be identified

ERYTHEMA MULTIFORME

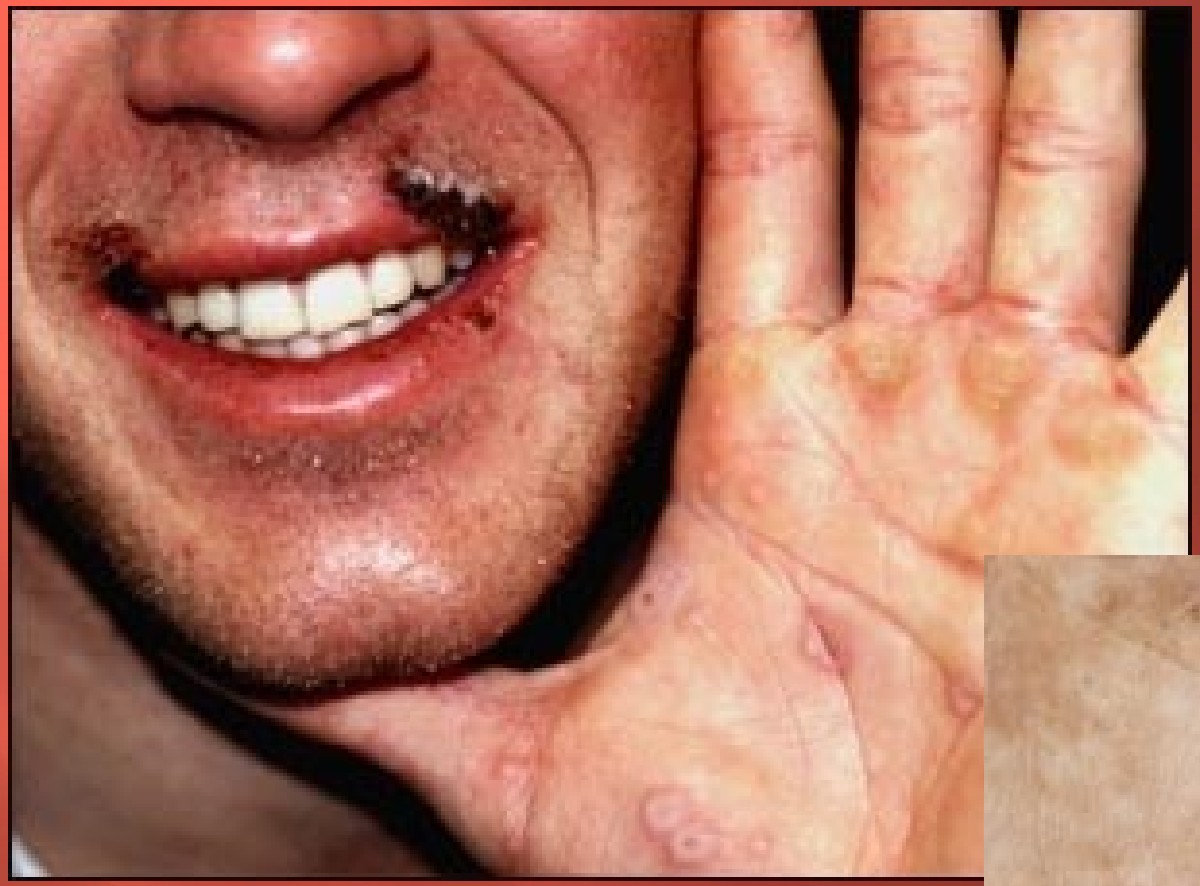
Iris and target-like patterns with concentric macules and papules on the palm

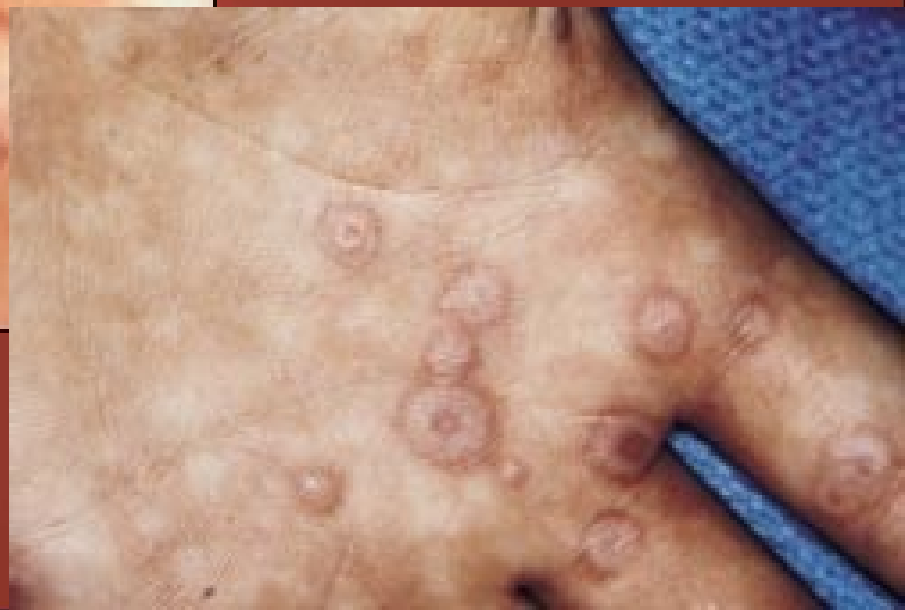




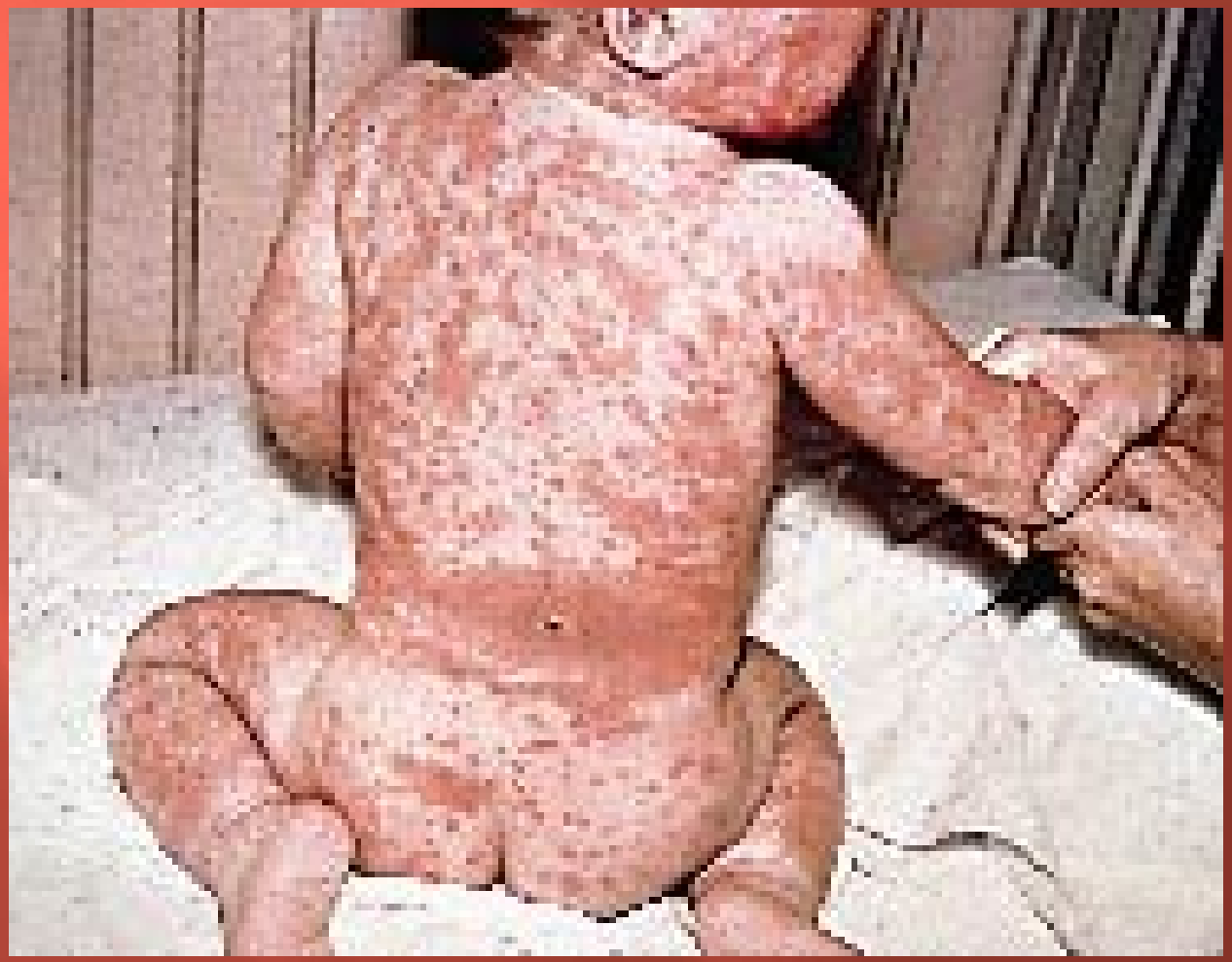
Multiple, confluent target-like papules and vesicles on the central facies. Bullae on the lips and the buccal mucosa.

ERYTHEMA MULTIFORME



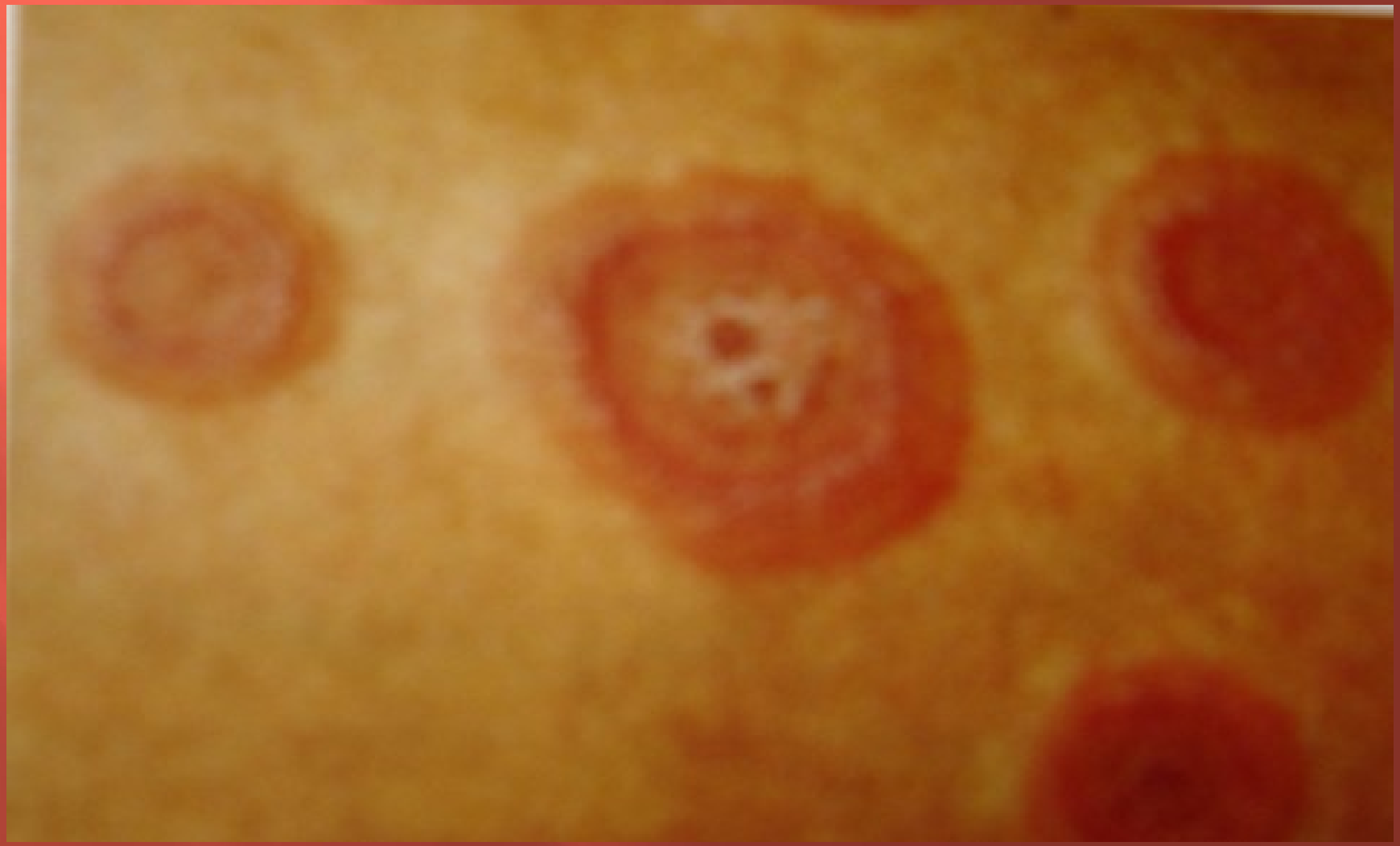


ERYTHEMA MULTIFORME MAJOR



Child with erythema multiforme, following smallpox vaccination

TARGET LESION



TREATMENT

- Symptomatic
- 1.Systemic Corticosteroid not Needed

- Recurrent EM
- Oral Acyclovir 200 mg 5 Times a Day for the treatment

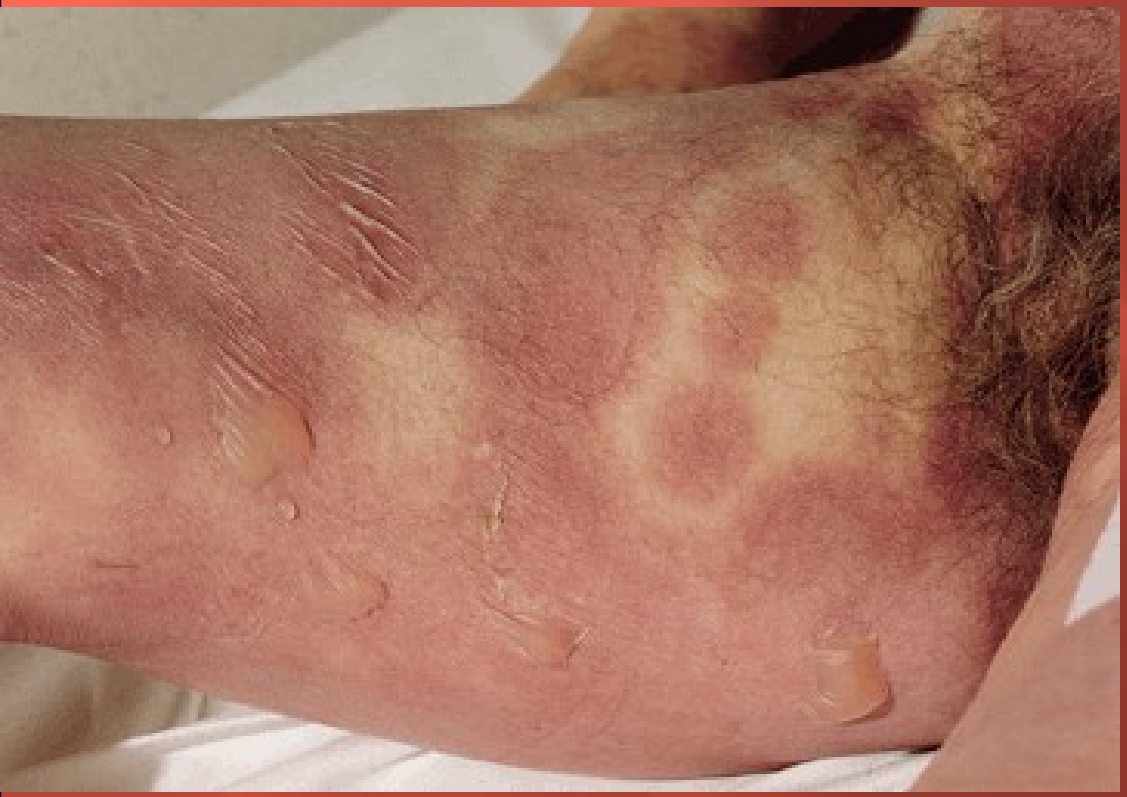
- Low Dose Acyclovir-
- 400-800 mg oral per day for 6 Month may be indicated

Risk factors for Drug Allergy

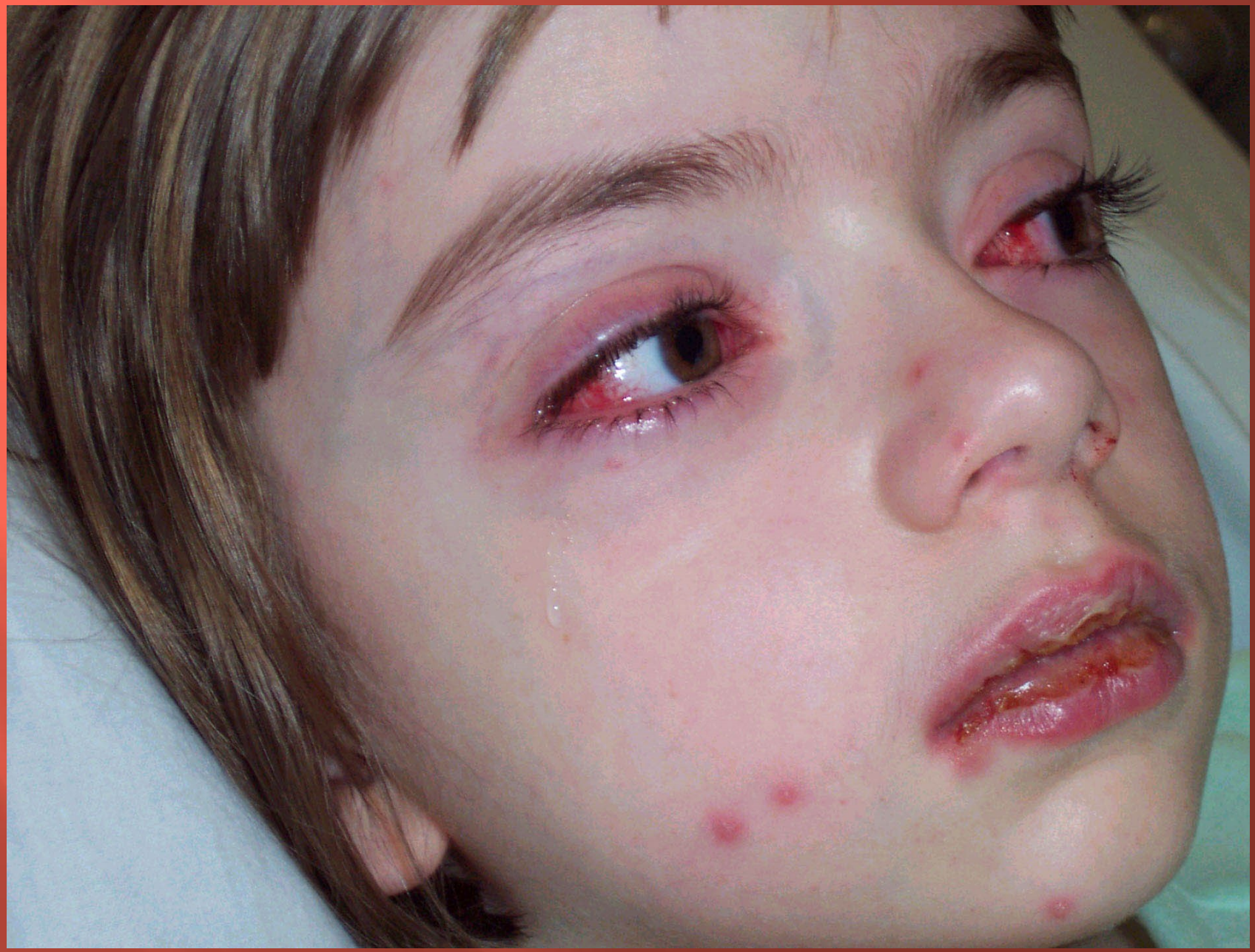
- Frequent exposure to the drug
- Large doses of the drug
- Drug given by injection rather than pill
- Family tendency to develop allergies and asthma.

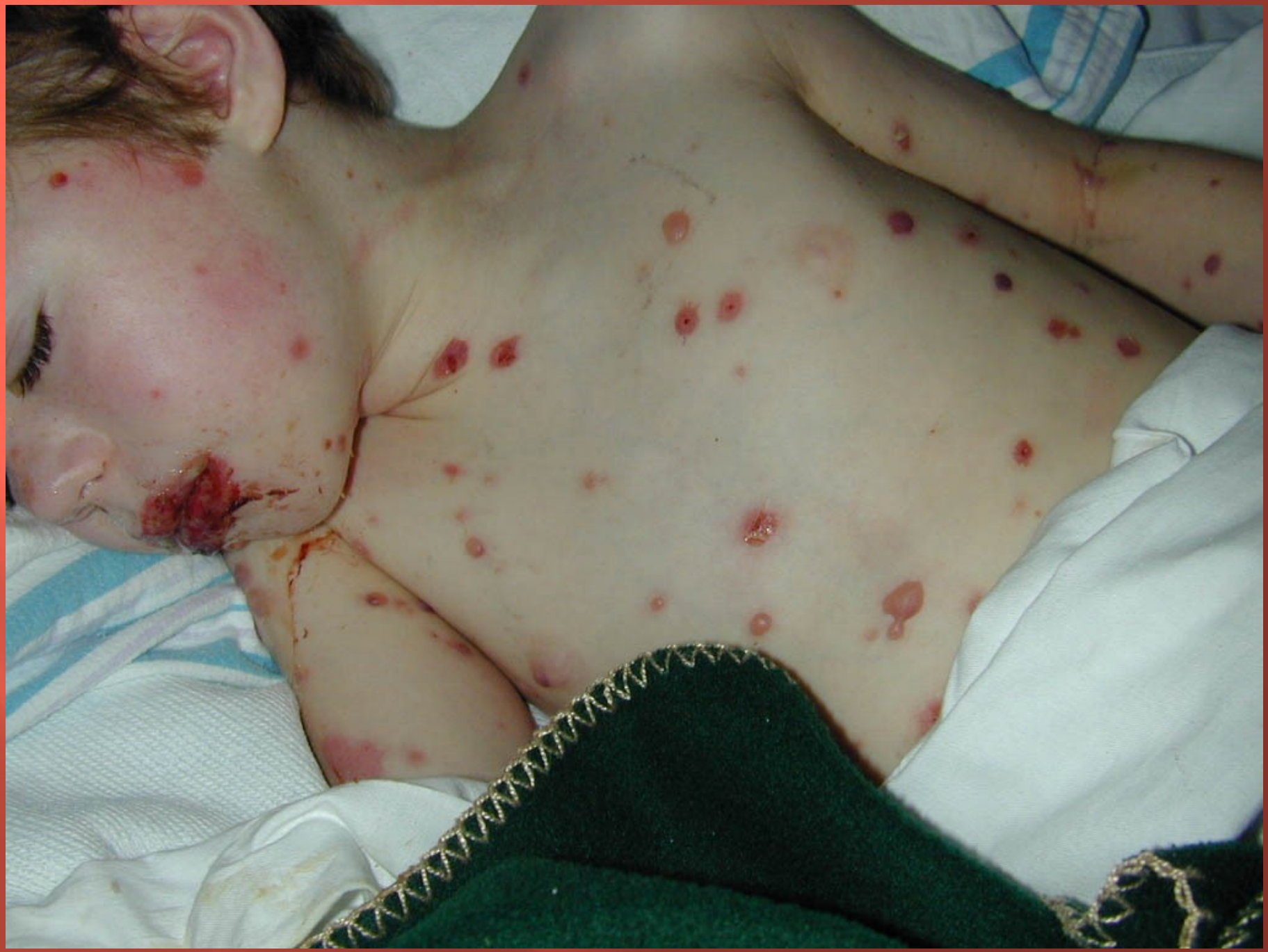
- Steven jhonson syndrome

STEVENS-JOHNSON SYNDROME

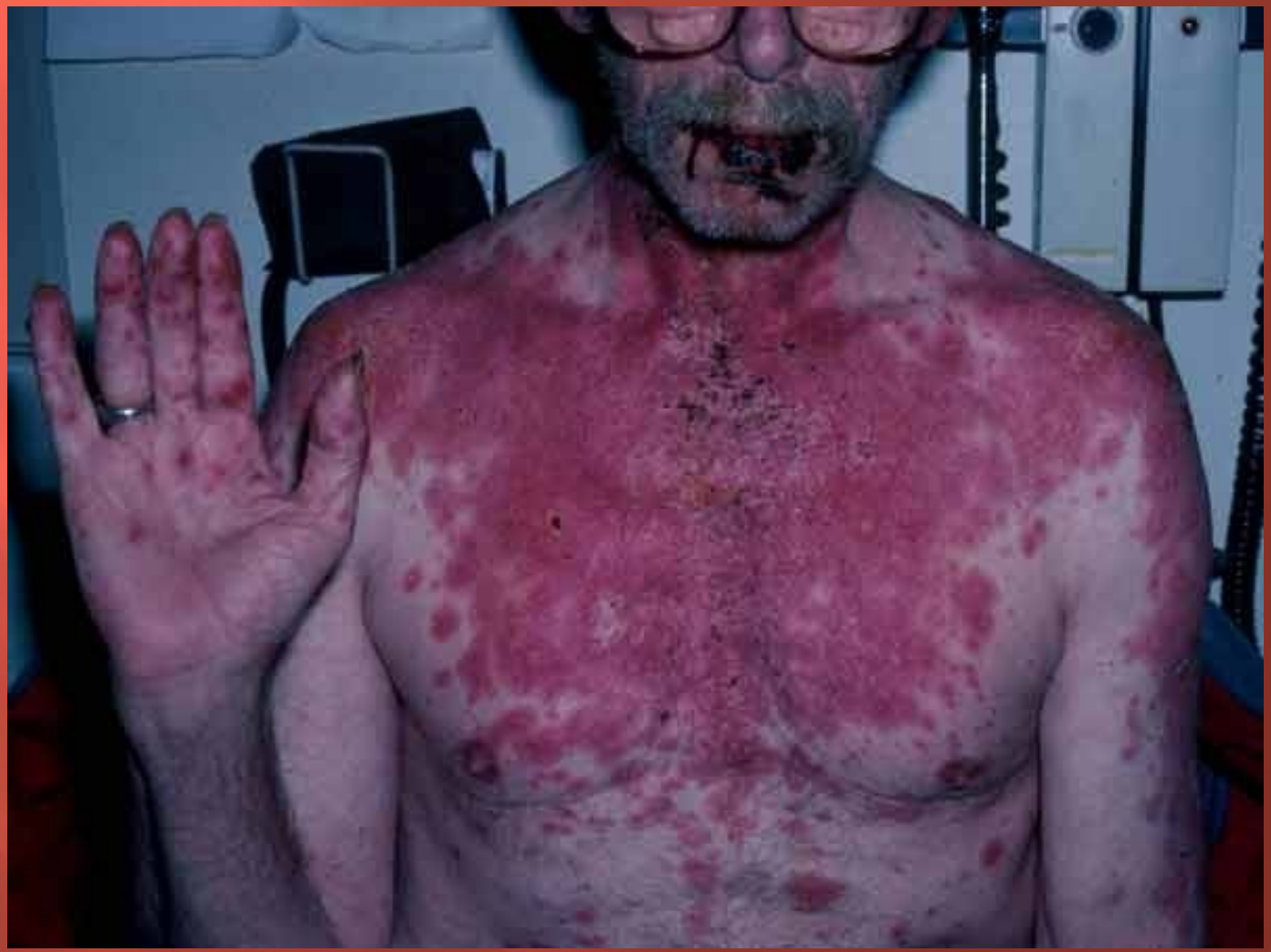


Generalized eruption of lesions that initially had a target-like appearance but then became confluent, brightly erythematous, and bullous. The patient had extensive mucous membrane involvement and tracheobronchitis.

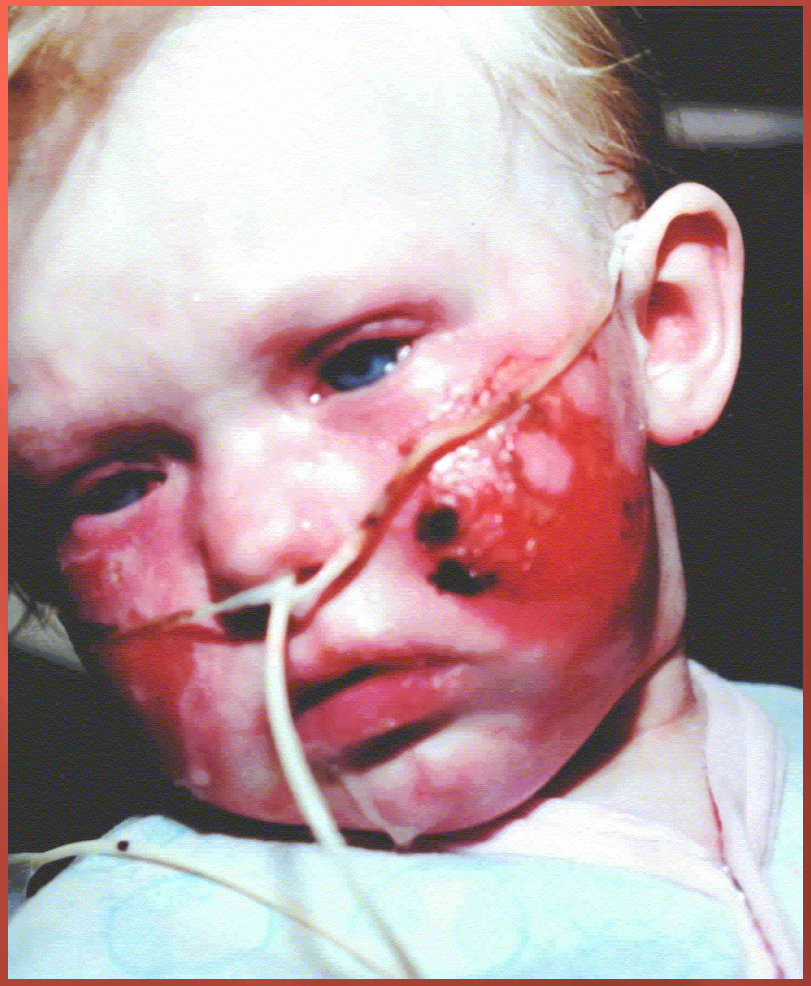


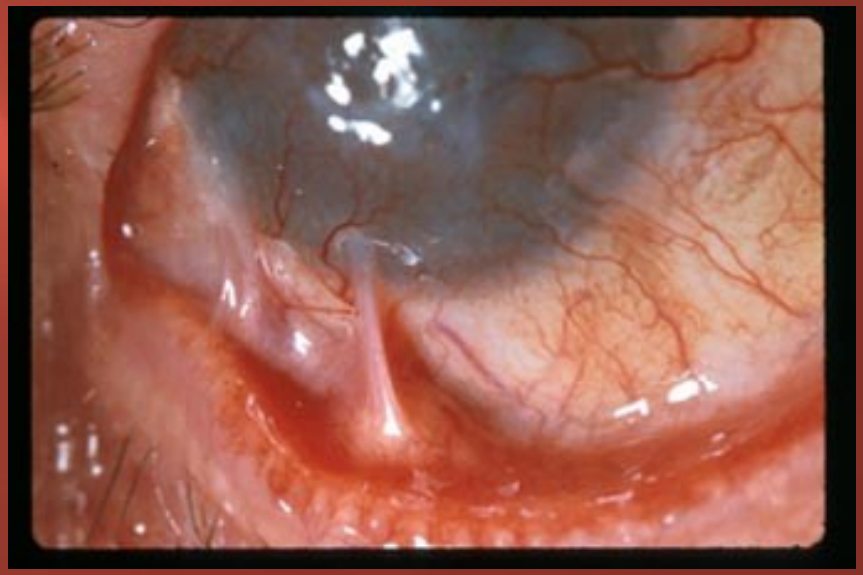


STEVENS-JOHNSON SYNDROME



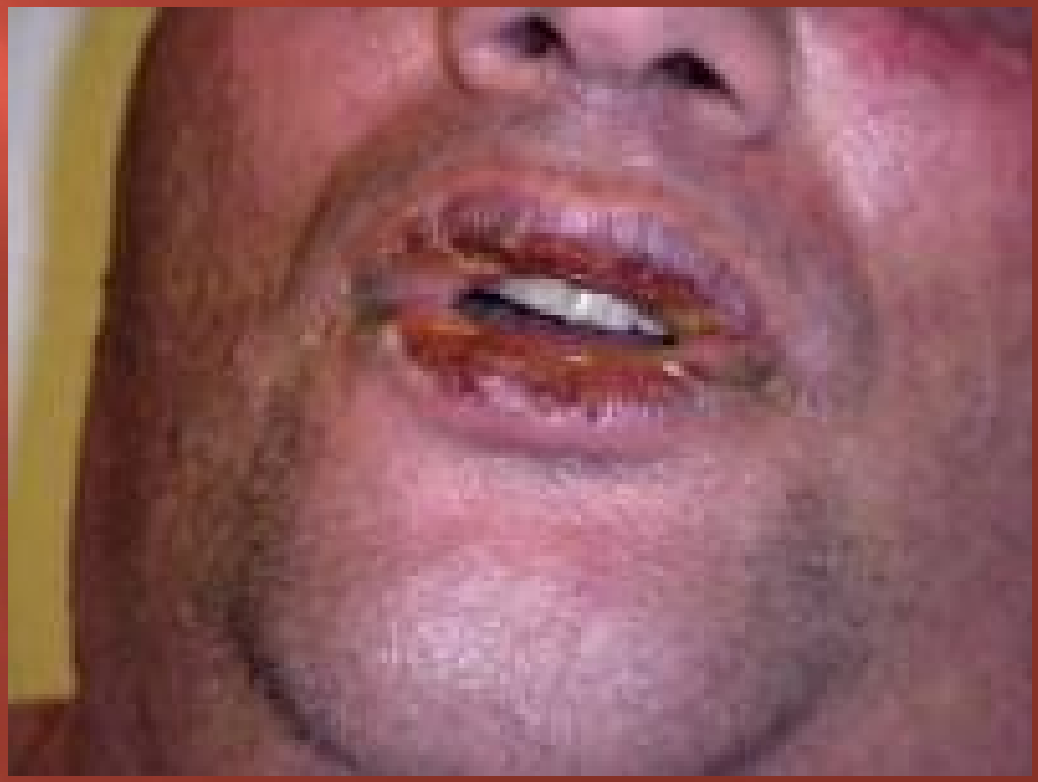
STEVENS-JOHNSON SYNDROME





Case 1: 55 yo male with hypertension, gout and Hyperlipidemia. He develops hemorrhagic blisters and a skin rash after starting a new medication. What is this?

- A) Angioedema
- B) Stevens-Johnson syndrome
- C)Toxic epidermal necrolysis
- D) Anaphylaxis
- E) Erythroderma



Case 1 (continued)

- What is the most likely drug to cause this?

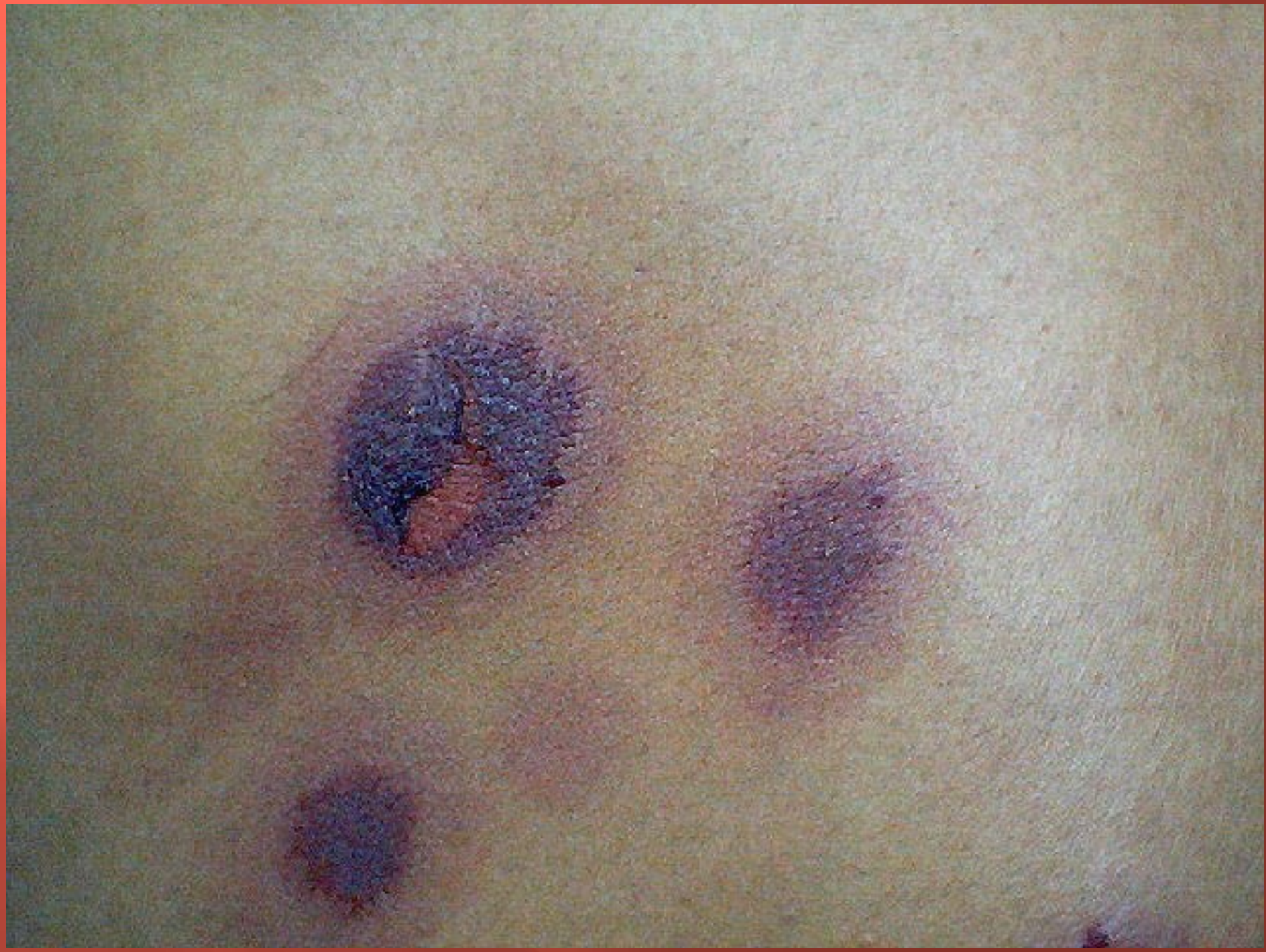
A) Hydrochlorothiazide
B) Cervuastatin
C) Allopurinol
D) Colchicine
E) Atenolol

DRUGS

- Sulphasalazine
- Co-Trimoxazole
- Hydantoins
- Carbamazepine
- Barbiturates
- Phenylbutazone
- Ibuprofen
- Piroxicam
- Allopurinol
- Aminopenicillens
- Fluroquinolones

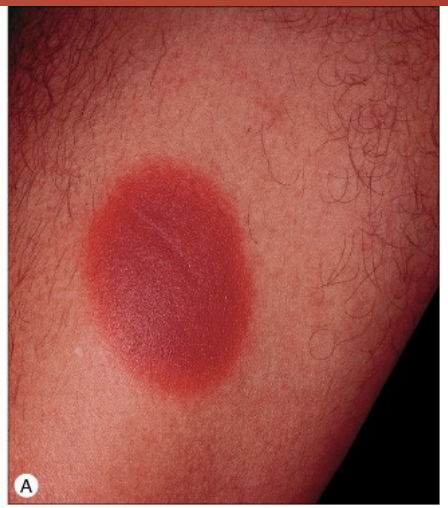
Fixed Drug Eruptions

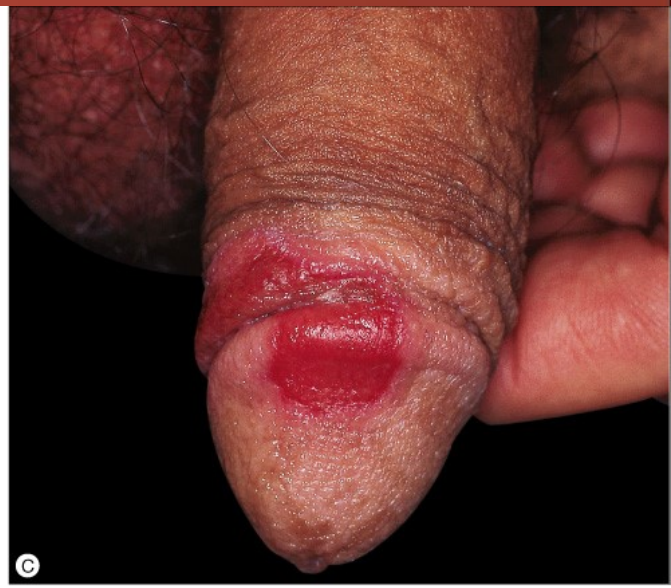
- Drug eruption that occurs at the same location every time a particular medication is used.
- Begins as an erythematous, edematous plaque with a grayish center or frank bullae, then progresses to dark, post-inflammatory pigmentation.
- Sites include the mouth, genetalia, face, and acral areas.
- Causes include phenolphthalein, tetracyclines, barbituates, sulfonamides, NSAIDs, and salicylates.

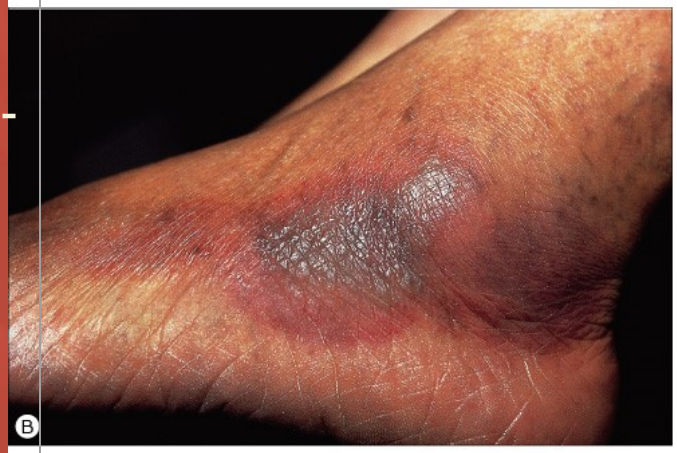


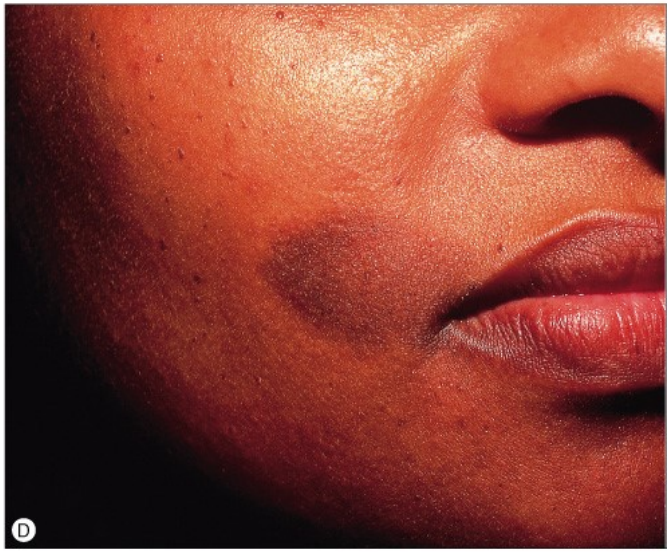
Fixed Drug Eruptions

Phenophthalein - A
naproxen - B ,
Ciprofloxin - C ,
TMP/sulfamethoxazole - D





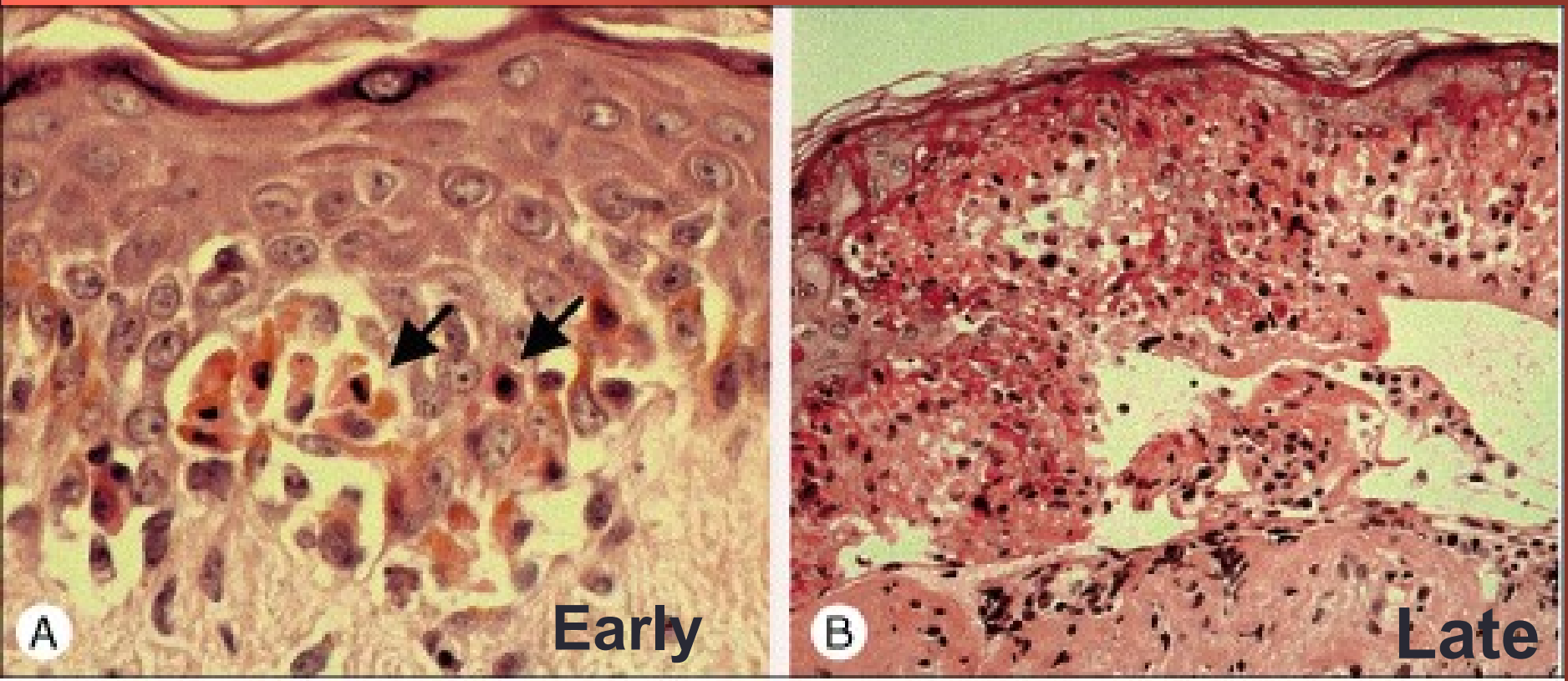




Bullous Drug Reactions

- Definition:
  - SJS < 10% of body surface area involved
  - 10-30% are overlap cases
  - >30 % TEN
- Likely a disease spectrum.

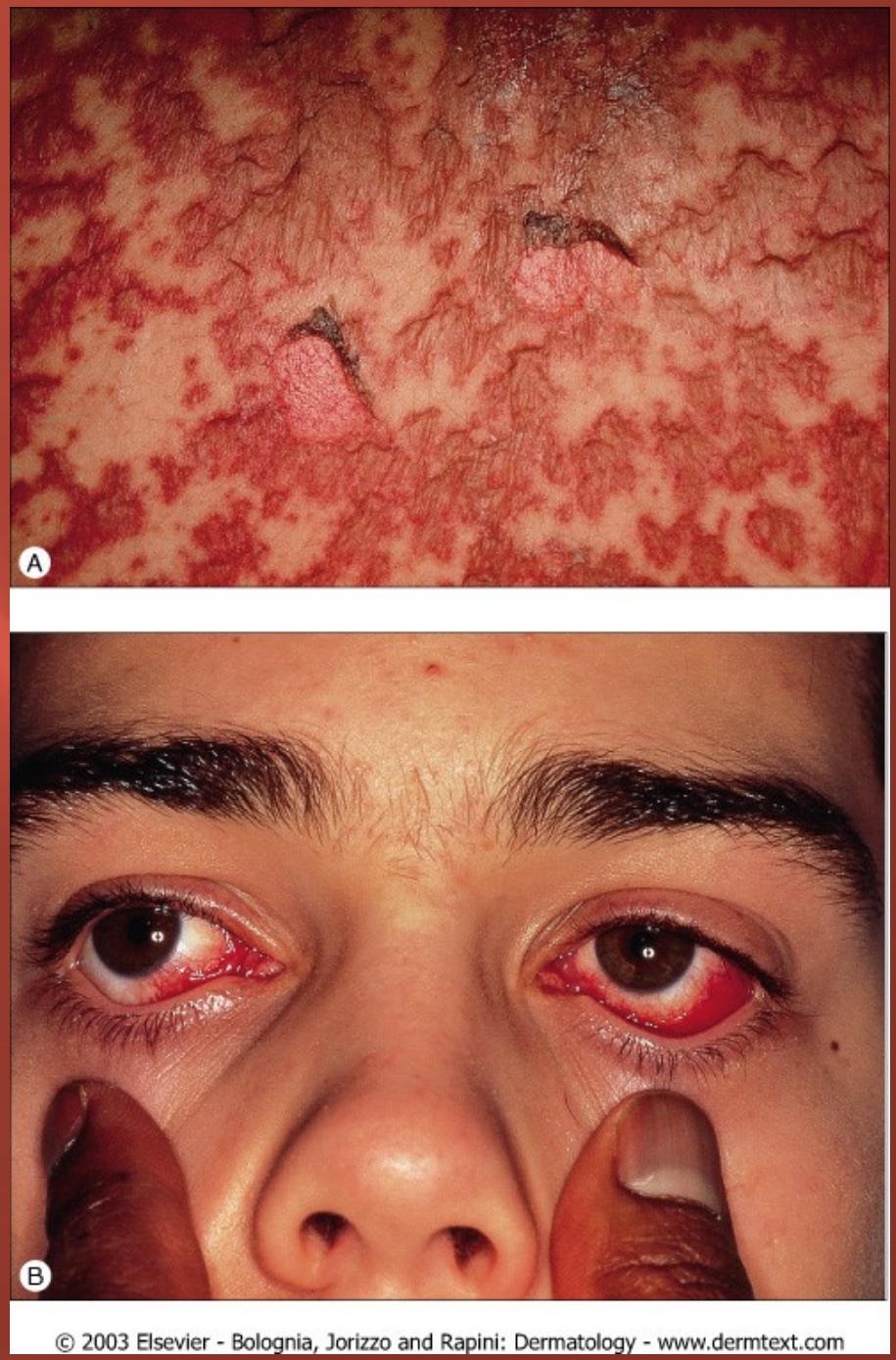
Histology of TENS

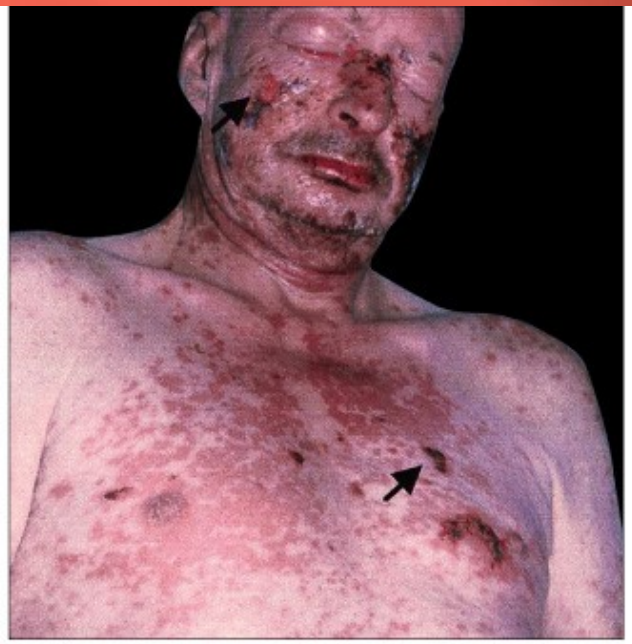


- A lymphocytic infiltrate at the D-E junction
- Necrosis of keratinocytes that may be full thickness
- Infiltrate may be marked or very scant

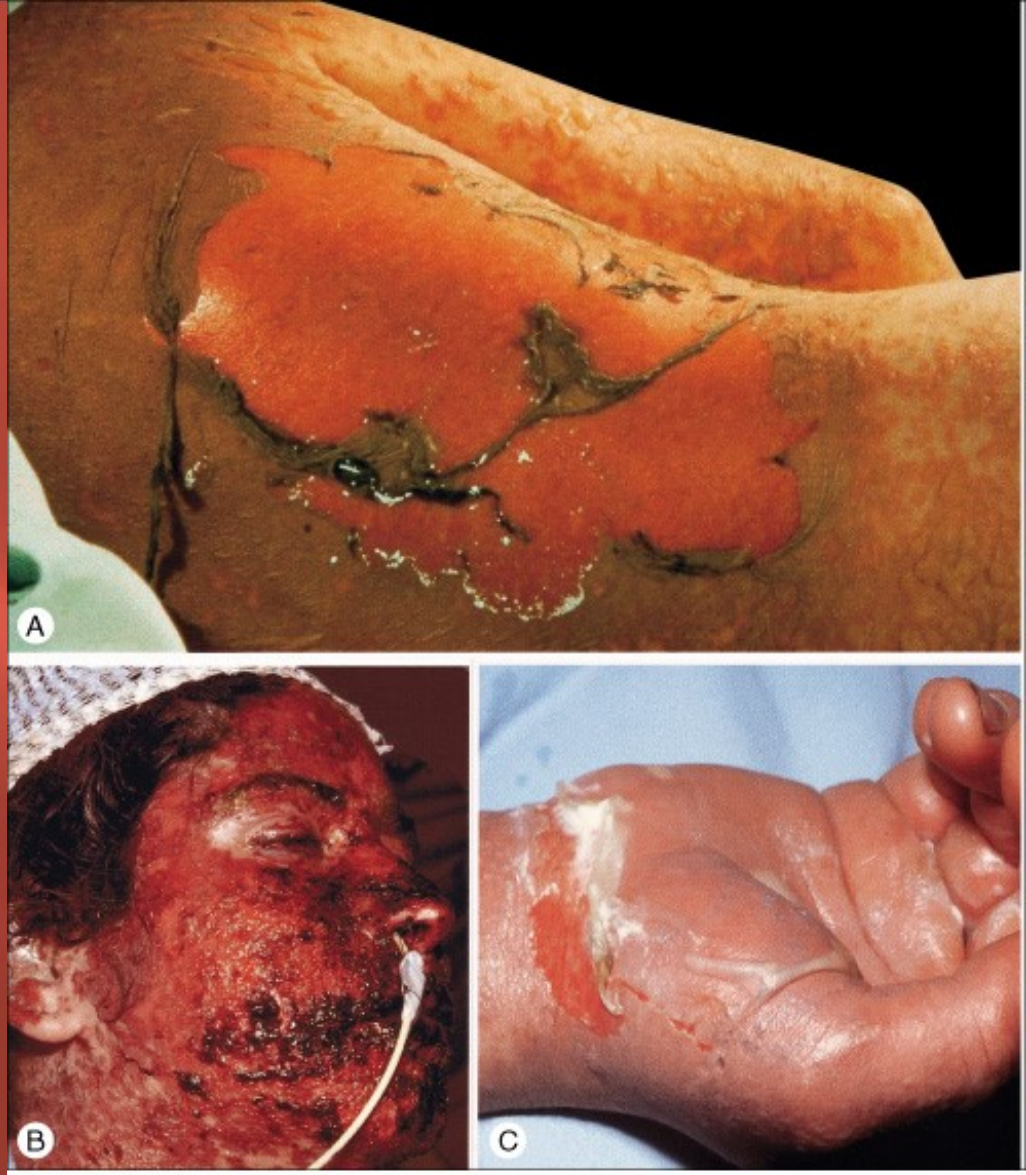
SJS

Skin and conjunctival Involvement



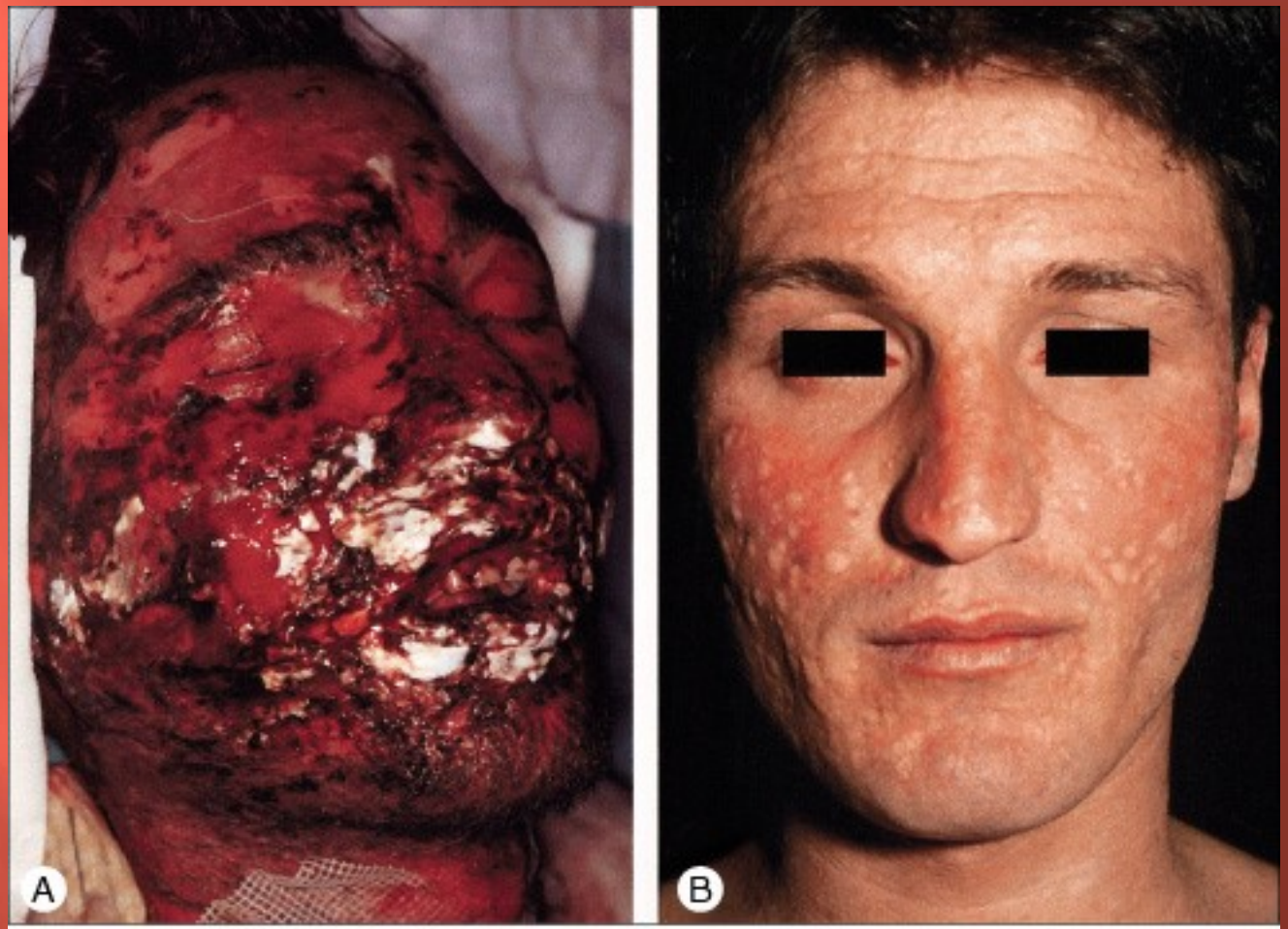


SJS



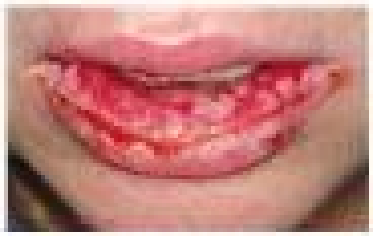
TENS

TEN

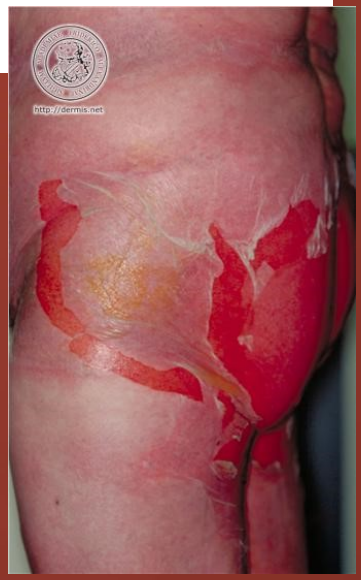


Three weeks of healing after receiving IVIG.

What is it, and is their skin going to fall off?



Skin rash + 2 or more mucosal sites



BSA: <10% 10-30% >30%

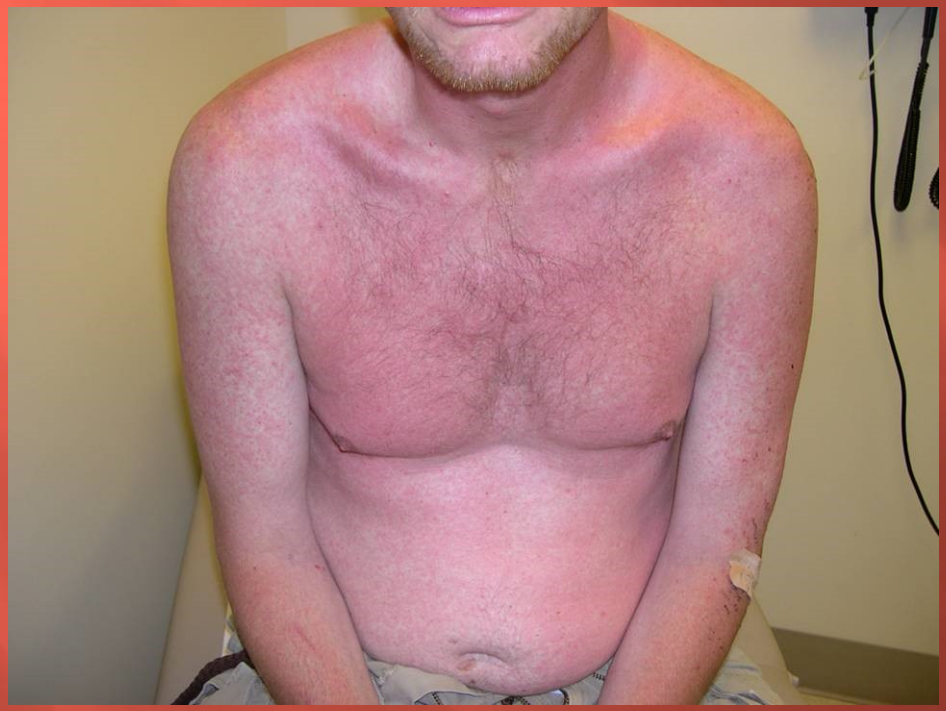
Stevens-Johnson

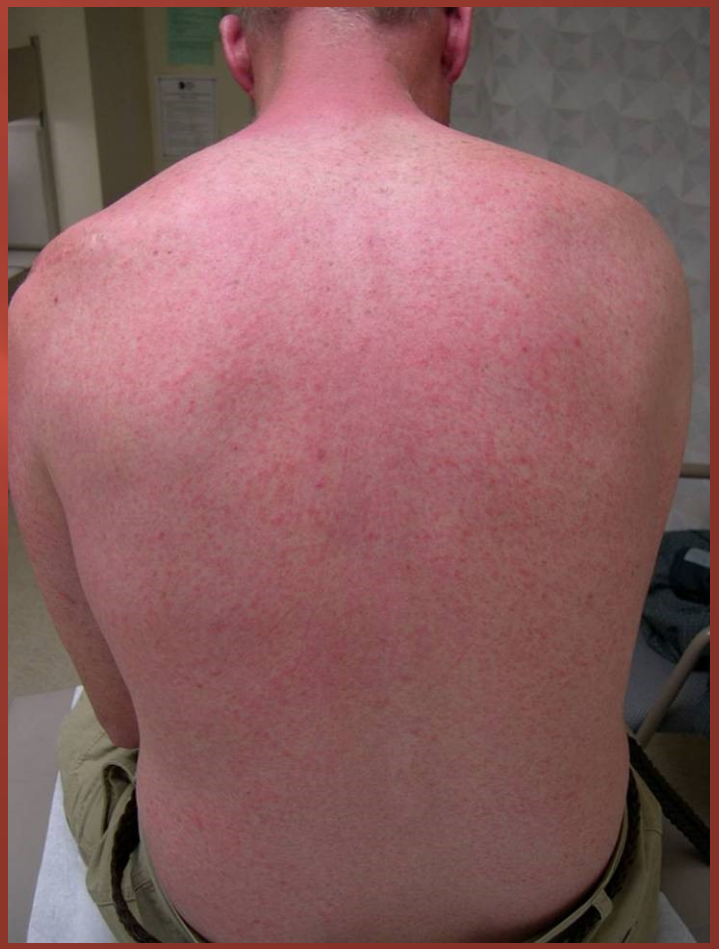
SJS/TEN overlap

TEN

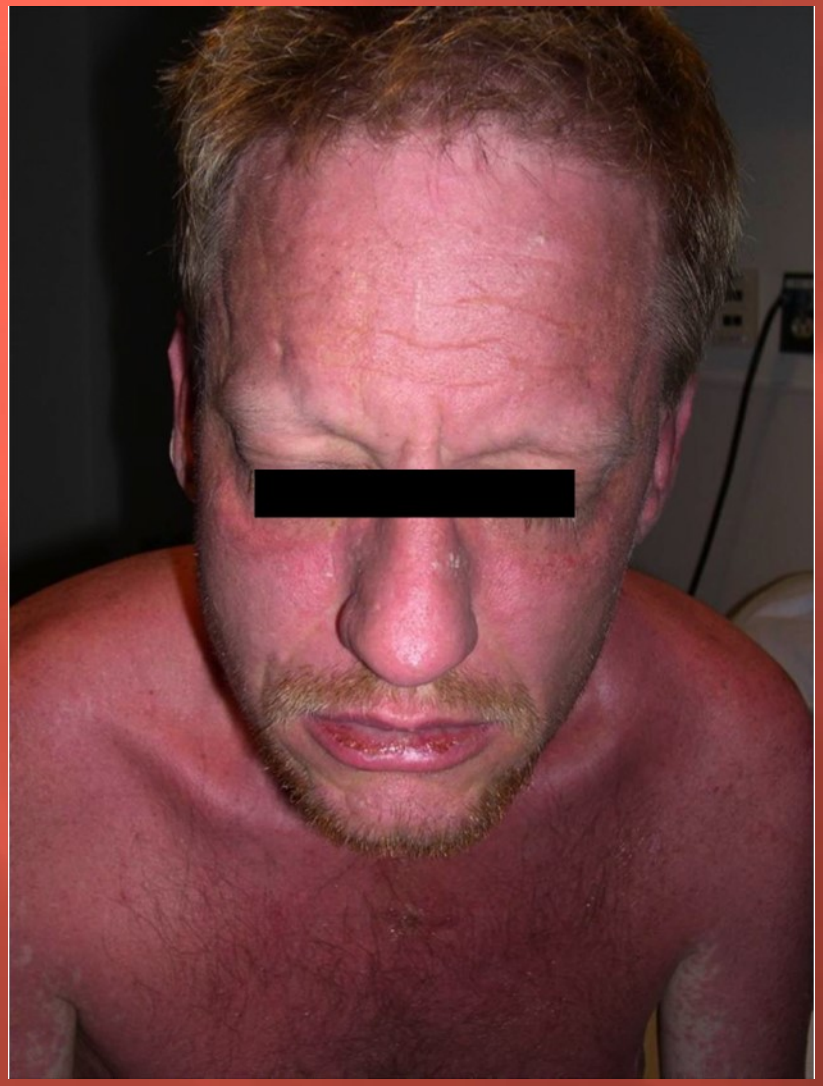
Mortality: 5-10% 30-50%

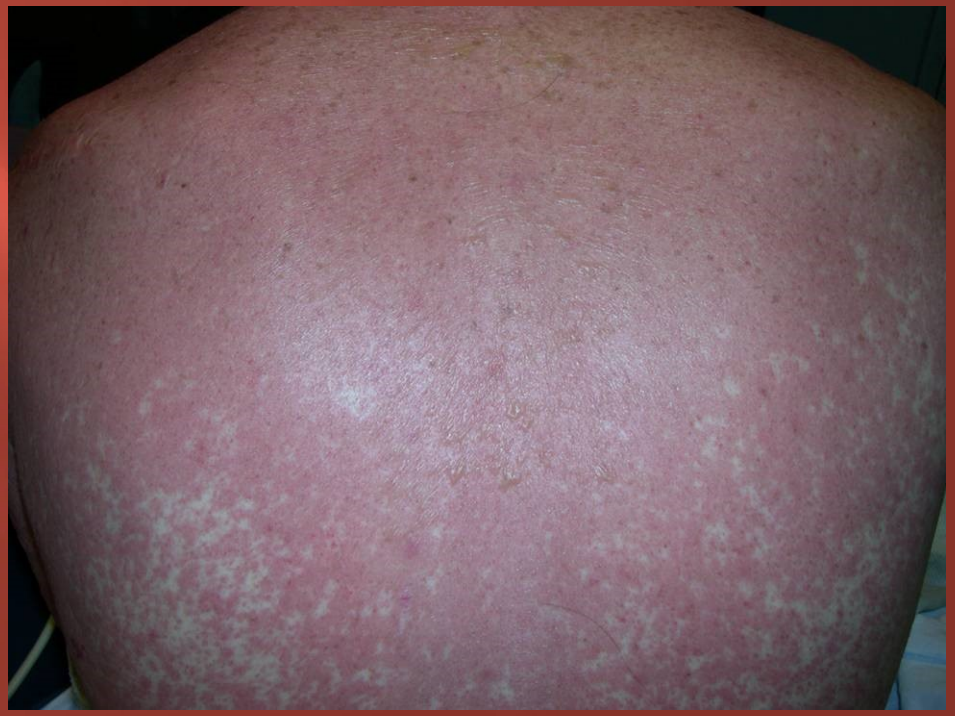
Day of Admit



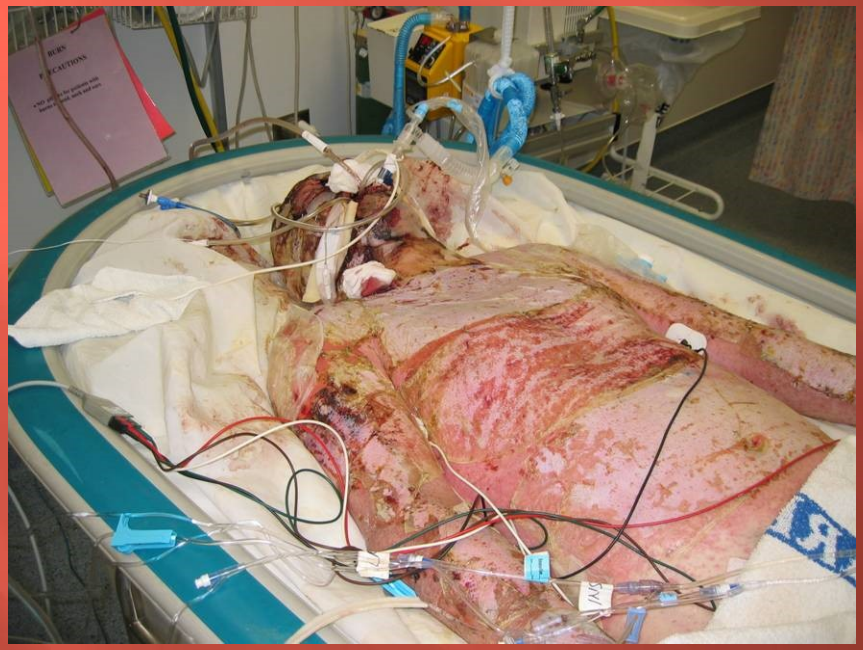


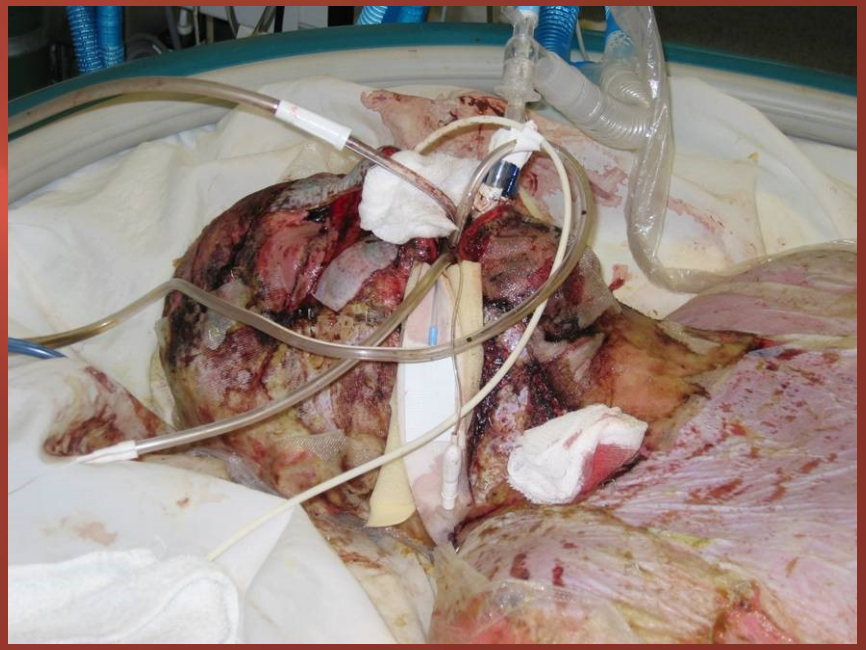
Day 2





Day 4



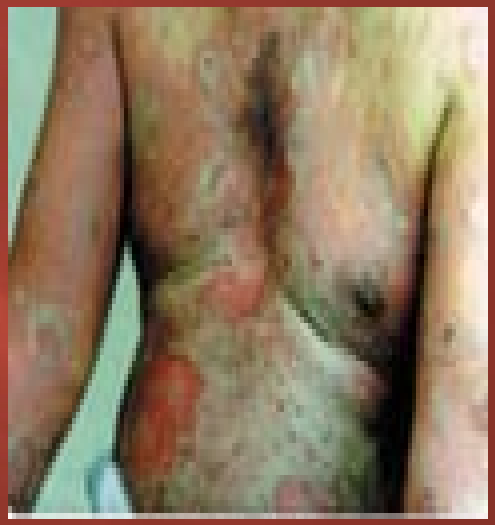


TOXIC EPIDERMAL NECROLYSIS

Introduction

TEN:

- Very rare and potentially fatal skin disorder.
- Usually triggered by immunological reaction
- Similar symptoms to burn patients.

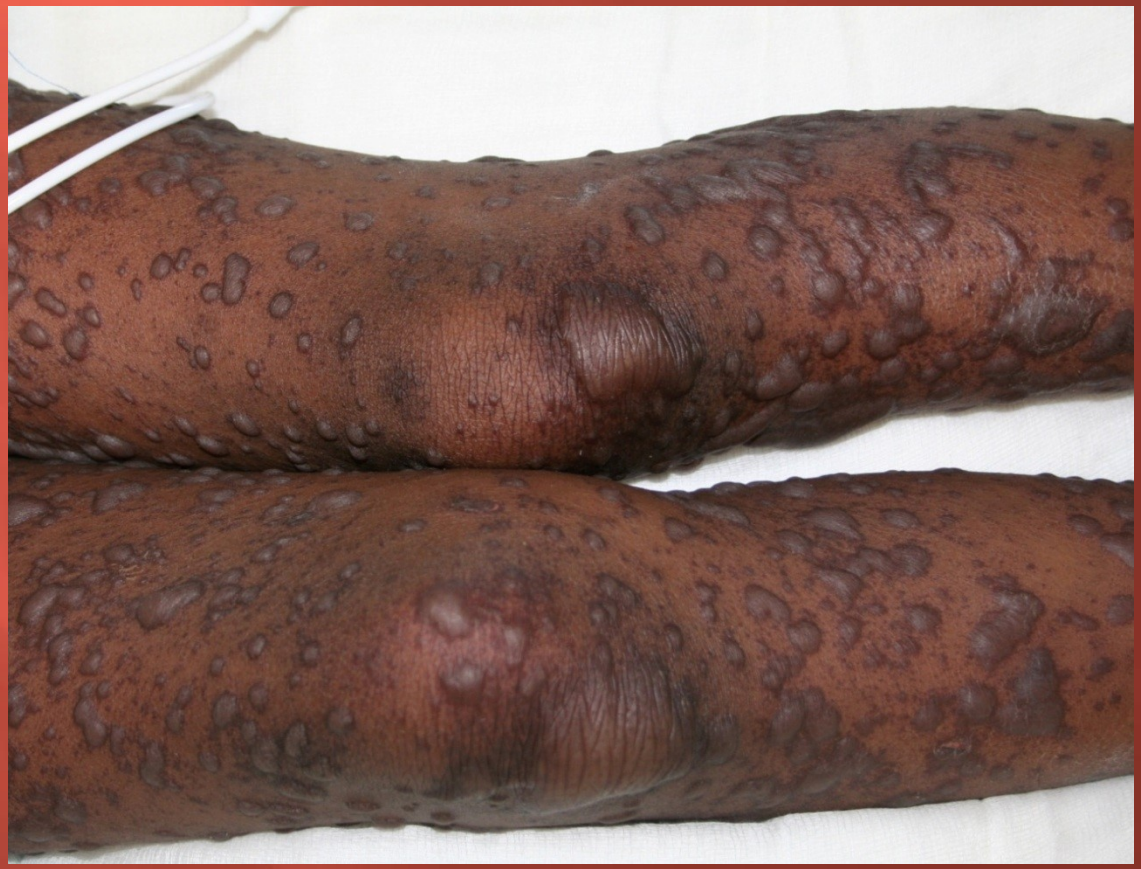


Causes of TEN

Caused by immune reaction to:

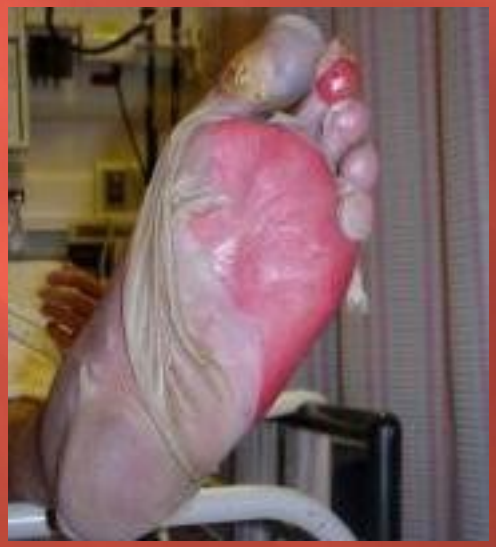
- Certain types of infections
  - *S. aureus, E.coli*
- Some vaccinations
  - Polio

Skin Bullae



Shedding Skin

SKIN STARTS SLOUGHING



SKIN COMPLETELY GONE

Who does it affect?

Affects:

- People of all ages.
- Both genders
  - Women more than men.
  - HIV, AIDS, etc.

Diagnosis

Final diagnosis is done by:

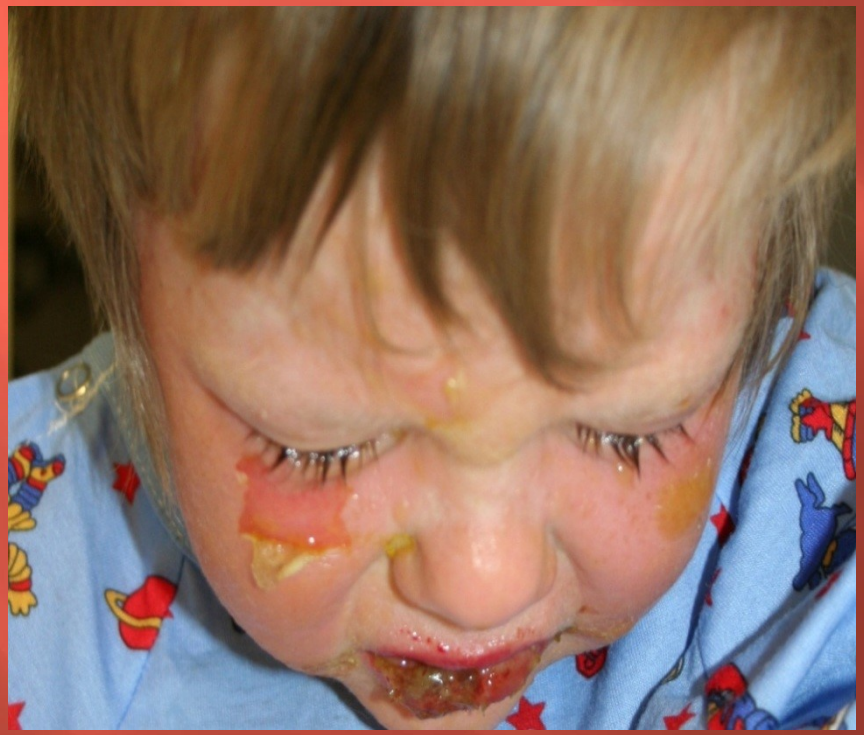
- Taking tissue samples from the nose, pharynx, and unruptured blisters of those suspected patients.
- Samples are then cultured and organism responsible is identified.

Mortality factors

- Mortality rates are between 10-70% for this condition.

- Factors include:
  - Dehydration
  - The initiation of treatment
  - Aggressiveness of treatment
  - Level of care
  - Amount of surface area involved
  - Cancer/hematologic malignancy

Complications



- Life-threatening sepsis.
  - Severe infection
- Keratoconjuctivitis
  - Leads to impaired vision and then blindness

Guideline for Treatment of SJS & TEN

- Admit to intensive care or burn unit
- Discontinue culprit medication and all unnecessary medications
- Sterile technique in handling patient
- Place intravenous or central line in area of uninvolved skin if possible

Guideline for Treatment of SJS & TEN

- 1.Culture skin, blood, urine daily
- 2.Avoid prophylactic systemic antibiotics and silver sulfadiazine to skin
- 3.Fluid and electrolyte monitoring and replacement
- 4.Initiate total parenteral nutrition or nasogastric feedings if unable to take po

Guideline for Treatment of SJS &TEN

- Remove oral and nasal debris daily; antiseptic mouthwashes or oral sprays daily
- Antiseptic eye drops daily and ophthalmology consultation
- Anticoagulation to prevent deep vein thrombosis and pulmonary embolism

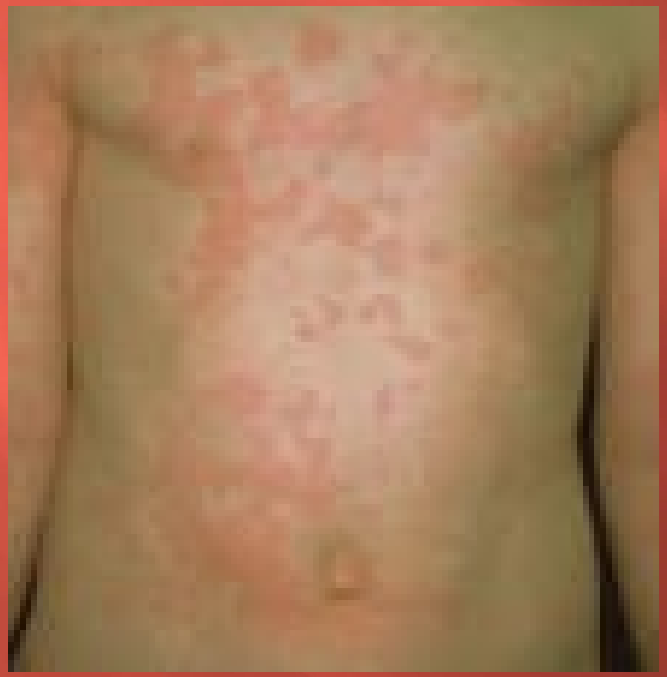
Treatment

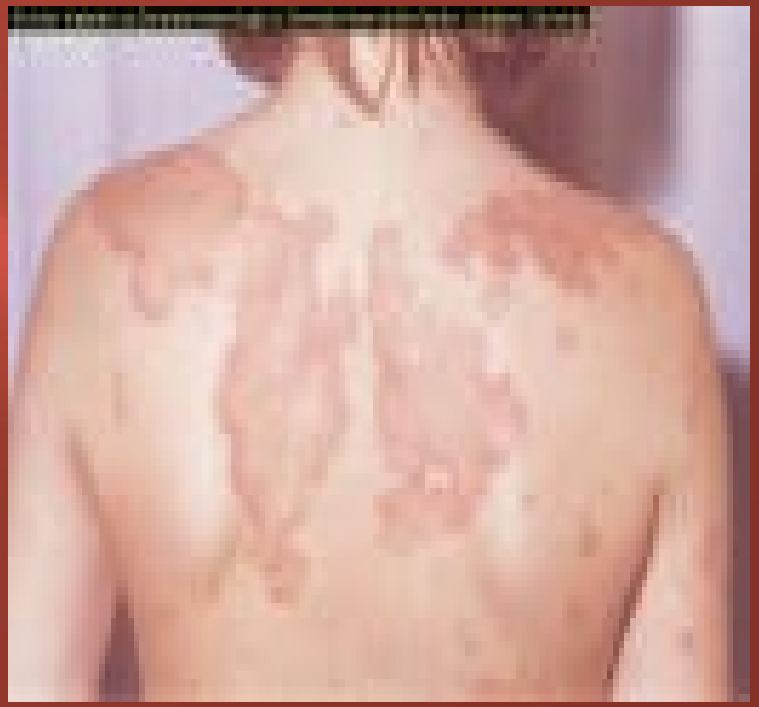
- Treatment is similar to that of severe burns
  - All suspicious meds are discontinued immediately.
  - Systemic antibiotic treatment with corticosteriods, used with extreme caution.

Urticaria

- What is urticaria?
- It is local wheals and erythema in the superficial dermis
- Urticaria induced by drug is generally acute and is limited to the skin and subcutaneous tissues.

Urticaria





Urticaria

- Treatment for acute urticaria
- 1.Symptoms subside in 1 to 7 days, treatment is chiefly palliative.
- 2.All nonessential drugs should be stopped until the reaction has subsided.
- 3.Symptoms can be relieved by oral antihistamine and glucocorticoid.

Drugs for Acute Urticaria

- Oral antihistamine: diphenhydramine 50-100mg q4h, hydroxyzine 25-100mg

- Glucocorticoid for more severe reactions, especially when associated with angioedema (prednisone 30-40 mg/ day po)

Angioedema

What is angioedema?

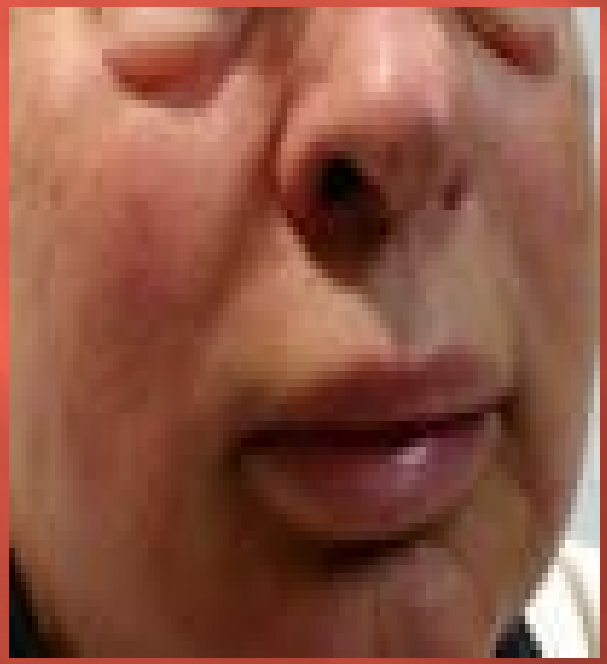
- It is a deeper swelling due to edematous areas in the deep dermis and subcutaneous tissue and may also involve mucous membranes.

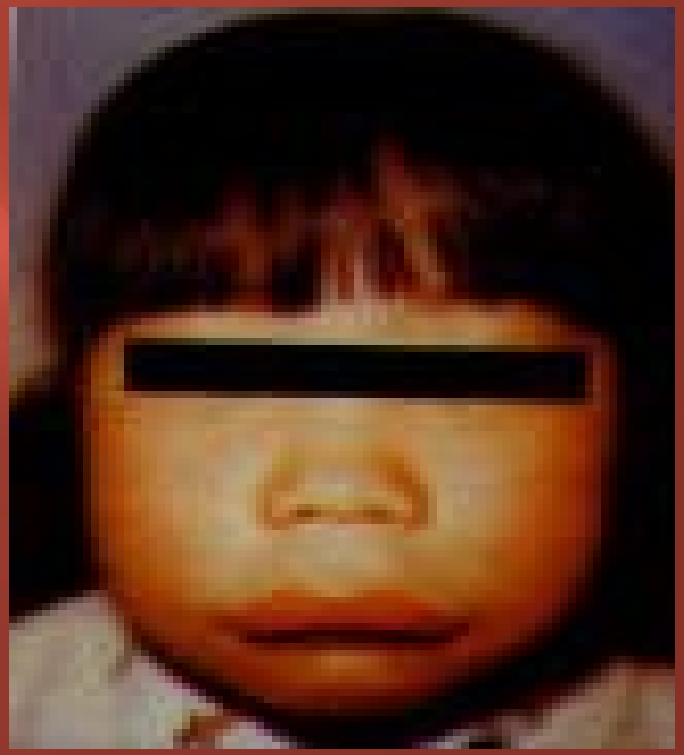
Signs & Symptoms of Angioedema

- Diffuse and painful swelling of loose subcutaneous tissue, dorsum of hands or feet, eyelids, lips, genitalia and mucous membranes.

- Edema of the upper airways may produce respiratory distress

Angioedema

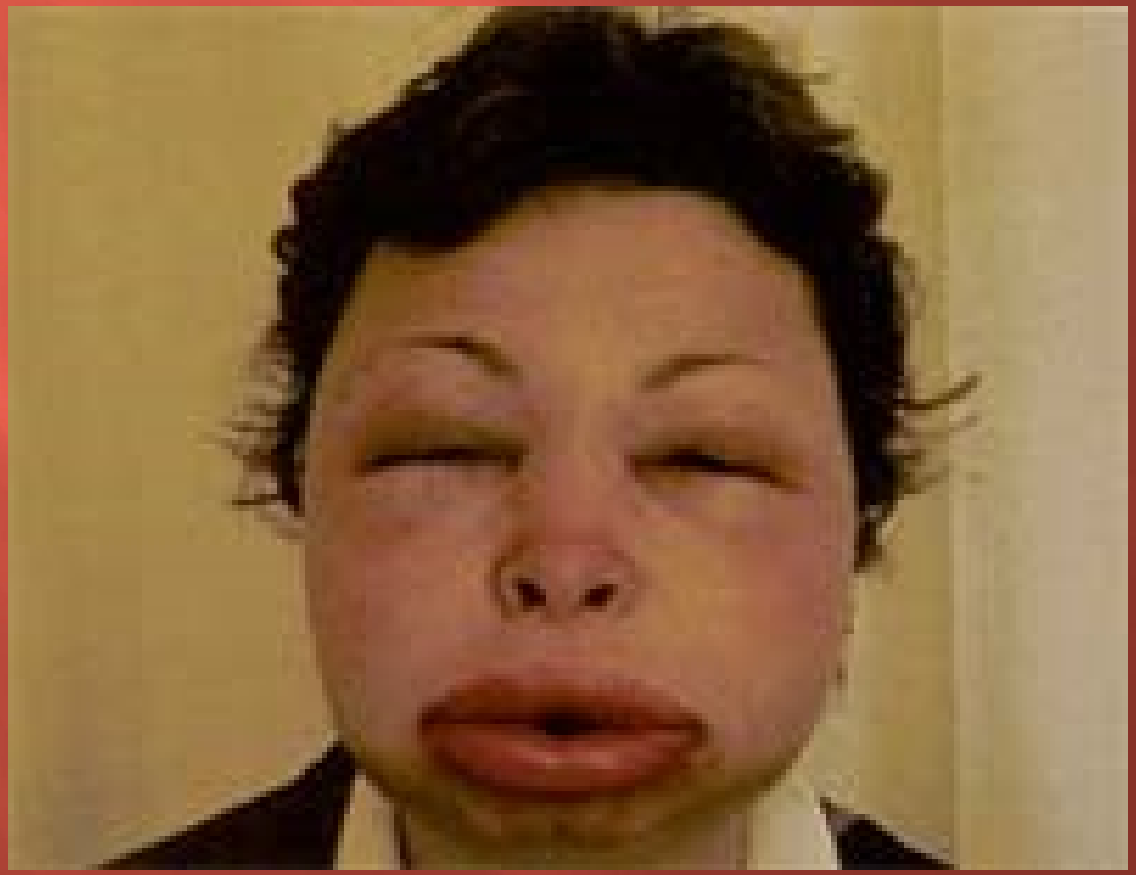




Management for Angioedema

- Glucocorticoid (e.g. prednisone 30-40mg/day po)
- Adrenaline 1:1000, 0.3ml subcutaneously should be the 1st line treatment for acute pharyngeal or laryngeal angioedema
- IV antihistamine (e.g. diphenhydramine 50-100mg) to prevent airway obstruction
- Intubations or tracheotomy and oxygen administration may be necessary

Case #3: 35 yo female with depression, hypertension and seizure disorder. Complains of acute wheezing and lip edema after starting a new medication



Case #3 (cont)

- What is the most likely Diagnosis?

- A) C1 esterase inhibitor deficiency
- B) Amyloidosis
- C) Acquired Angioedema
- D) Anaphylaxis
- E) Erysipelas

DRUG REACTIONS

Amiodarone

<u>Drug-induced pigmentation</u>:
Striking slate-gray pigmentation in facial distribution.
Blue color (ceruloderma) is due to deposition of melanin contained in macrophages and endothelial cells in the dermis.
Pigmentation is reversible, but it may take > 1 year!
In this patient it took 33 months for the ceruloderma to disappear.

Drug induced pigmentation